

CLAIMS

1. A pharmaceutical composition, said composition comprising a therapeutically effective amount of a compound of the formula R-COOH, or a salt or an ester or amide of such compound, where R designates a saturated or unsaturated alkyl chain of 10-24 carbon atoms, one or more of which may be replaced by heteroatoms, where one or more of said carbon or heteroatom chain members optionally forms part of a ring, and where said chain is optionally substituted by a hydrocarbyl radical, heterocyclyl radical, lower alkoxy, hydroxyl-substituted lower alkyl, hydroxyl, carboxyl, halogen, phenyl or (hydroxy-, lower alkyl-, lower alkoxy-, lower alkenyl- or lower alkinyl)-substituted phenyl, 10 C₃-C₇ cycloalkyl or (hydroxy-, lower alkyl-, lower alkoxy-, lower alkenyl- or lower alkinyl)-substituted C₃-C₇ cycloalkyl wherein said compound is capable of being endogenously converted to its respective coenzyme A thioester, RCOSCoA.

2. A composition according to claim 1, wherein R is selected from the group 15 consisting of ω -carboxyl, ω -hydroxyl boron, and ω -hydroxyl chains.

3. A composition according to claim 1, where RCOOH is either clofibrlic acid or fibrlic acid, or a salt, ester, amide, or derivative thereof.

20 4. A composition according to claim 1, where RCOOH is a nonsteroidal antiinflammatory drug (NSAID).

5. A composition according to claim 1, where RCOOH is a saturated or unsaturated long chain fatty acid.

5 6. A composition according to claim 5, where the fatty acid is chosen from:

Stearic(18:0) acid
Oléic(18:1) acid
Linolenic(18:2) acid
Linolenic(18:3) acid
Eicosapentaenic(20:5) acid
Docosahexaenic(22:6) acid

7. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

1,16 Hexadecanedioic acid
1,18 Octadecanedioic acid
2,2,15,15-tetramethyl-hexadecane-1,16-dioic acid
2,2,17,17-tetramethyl-octadecane-1,18-dioic acid
3,3,14,14-tetramethyl-hexadecane-1,16-dioic acid
20 3,3,16,16-tetramethyl-octadecane-1,18-dioic acid
4,4,13,13-tetramethyl-hexadecane-1,16-dioic acid and
4,4,15,15-tetramethyl-octadecane-1,18-dioic acid

25 8. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

16-B(OH)2-hexadecanoic acid
18- B(OH)2-octadecanoic acid
16- B(OH)2-2,2-dimethyl-hexadecanoic acid

18- B(OH)2-2,2-dimethyl-octadecanoic acid
16- B(OH)2-3,3-dimethyl-hexadecanoic acid
18- B(OH)2-3,3-dimethyl-octadecanoic acid
16- B(OH)2-4,4-dimethyl-hexadecanoic acid
5 18- B(OH)2-4,4-dimethyl-octadecanoic acid

9. A composition according to claim 1, wherein RCOOH is selected from the group consisting of:

10 16-hydroxy-hexadecanoic acid
18-hydroxy-octadecanoic acid
16-hydroxy-2,2-dimethyl-hexadecanoic acid
18-hydroxy-2,2-dimethyl-octadecanoic acid
16-hydroxy-3,3-dimethyl-hexadecanoic acid
18-hydroxy-3,3-dimethyl-octadecanoic acid
15 16-hydroxy-4,4-dimethyl-hexadecanoic acid
18-hydroxy-4,4-dimethyl-octadecanoic acid

10. A method of treating an HNF-4 mediated disease state which method comprises administering a therapeutically effective amount of a compound which
20 inhibits HNF-4 controlled transcription.

11. A method of claim 10 wherein said compound comprises an amphipathic carboxylate capable of being converted to its respective CoA thioester.

25 12. A method of claim 11 wherein said amphipathic carboxylate is a xenobiotic amphipathic carboxylate.

13. A method of claim 10 wherein said compound shifts the HNF-4 dimer-oligomer equilibrium to favor an oligomer.

5 14. A method of claim 10 wherein said compound decreases the binding affinity of the HNF-4 dimer for a target gene.

10 15. A method of claim 11 wherein said amphipathic carboxylate is a C18:3 fatty acid.

16. A method of claim 11 wherein said amphipathic carboxylate is a C20:5 fatty acid.

17. A method of claim 10 for the treatment of Syndrome X.

15 18. A method of claim 10 for the treatment of coronary or peripheral atherosclerosis.

19. A method of claim 10 for the treatment of rheumatoid arthritis, multiple sclerosis, psoriasis or inflammatory bowel diseases.

20 20. A method of claim 10 for the treatment of breast cancer, colon cancer or prostate cancer.

21. A method of modulating HNF-4 transcriptional activity in vivo comprising exposing the HNF-4 or a nucleic acid encoding HNF-4 to an effective amount of an amphipathic carboxylate, an antisense molecule, a ribozyme, or an antibody for HNF-4 or its gene.

5 22. A method of claim 21 wherein said amphipathic carboxylate is a fatty acid capable of being converted to its respective CoA thioester.

23. A method of claim 21 wherein said modulation is inhibition of HNF-4 activity.

24. A method of claim 21 wherein said modulation is activation of HNF-4 activity.

10 25. A method of claim 21 wherein said amphipathic carboxylate is a C18:3 fatty acid.

26. A method of claim 21 wherein said amphipathic carboxylate is a C20:5 fatty acid.

15 27. A method of claim 21 wherein the modulation is via antibody interaction.

28. A method of claim 10 wherein said compound is an antisense molecule, a ribozyme, or an antibody to HNF-4.